PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US2004/011965	16.04.2004	30.09.2003

International Patent Classification (IPC) or both national classification and IPC
C12N15/82, C07K14/56, A01H5/00

Applicant
BIOLEX, INC.

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☒ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notifed the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:

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Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material:

   ☒ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☒ in written format

   ☒ in computer readable form

   c. time of filing/furnishing:

   ☐ contained in the international application as filed.

   ☐ filed together with the international application in computer readable form.

   ☒ furnished subsequently to this Authority for the purposes of search.

3. ☒ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

Box No. IV Lack of unity of invention

1. ☐ In response to the invitation (Form PCT/ISA/206) to pay additional fees, the applicant has:

   ☐ paid additional fees.

   ☐ paid additional fees under protest.

   ☐ not paid additional fees.

2. ☒ This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rule 13.1, 13.2 and 13.3 is

   ☐ complied with

   ☒ not complied with for the following reasons:

   see separate sheet

4. Consequently, this report has been established in respect of the following parts of the international application:

   ☒ all parts.

   ☐ the parts relating to claims Nos.

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	24-34
	No:	Claims	1-23
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-34
Industrial applicability (IA)	Yes:	Claims	1-34
	No:	Claims	

2. Citations and explanations

   see separate sheet

Re Item IV

Lack of unity of invention

1. Article 3(4)iii PCT and Rule 13.2 PCT stipulate that where a group of inventions is claimed the requirements of unity shall be fulfilled only where there is a technical relationship among those inventions involving one or more of the same corresponding special technical features. "Special" technical features are those features that define a contribution which each of the inventions makes over the prior art.

2. The only corresponding technical feature linking the different groups of inventions is that they all relate to truncated but biologically active alpha interferon variants. Such variants, however, were already known from the prior art (e.g Levy *et al.*, 1981, Gasdaska *et al.*, 2003, WO-0210414, WO-0243650) Therefore, this feature cannot provide a common inventive concept for inventions 1 - 5.

3. Consequently, there is lack of unity, and the different inventions not belonging to a common inventive concept, have been divided into different groups pursuant to Article 17(3)(a) PCT.

   Invention 1: Claims 1 - 34 (all partially),
   relating to a truncated human alpha-interferon (SEQ ID NOs:1 and 6), polynucleotides encoding said interferon and compositions comprising said interferon.

   Invention 2: Claims 1 - 34 (all partially),
   relating to a truncated human alpha-interferon (SEQ ID NOs:2 and 7), polynucleotides encoding said interferon and compositions comprising said interferon.

   Invention 3: Claims 1 - 34 (all partially),
   relating to a truncated human alpha-interferon (SEQ ID NOs:3 and 8), polynucleotides encoding said interferon and compositions comprising said interferon.

   Invention 4: Claims 1 - 34 (all partially),
   relating to a truncated human alpha-interferon (SEQ ID NOs:4 and 9),

polynucleotides encoding said interferon and compositions comprising said interferon.

Invention 5: Claims 1 - 34 (all partially),
relating to a truncated human alpha-interferon (SEQ ID NOs:5 and 10), polynucleotides encoding said interferon and compositions comprising said interferon.

4. The lack of unity will, however, not be further pursued. It may have to be reconsidered during national or regional phases.

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Article 33(2) PCT (Novelty)

1.1 The following documents (D) are referred to; the numbering is following the order of the International Search Report:

D1 Gasdaska *et al.*, 2003. Bioprocess. J. 2:49-55
D2 WO-02010414 (Biolex)
D3 Levy *et al.*, 1981. PNAS 78:6186-6190
D4 WO-0243650 (Virogene)

1.2 Present claim 1 is directed to purified human alpha interferon polypeptides with C-terminal truncations of 4 - 8 amino acids.

1.3 Document D1 discloses a purified human alpha interferon polypeptide with a 7 amino acid truncation at the C-terminus. D1 thus anticipates the subject-matter of present claim 1. The same holds true for present claims 2 and 13 and for dependent claims 6, 11, 13 and 14 - 23. They do not meet the requirements of Article 33(2) PCT.

2. Article 33(3) PCT (Inventive step)

2.1 Present claims 24 - 34 do not contain any features that would merit an inventive step over the prior art D1 - D4.

2.2 The applicant is requested to note that even if formal novelty could be established for present claim 1, it still would lack an inventive step.

2.3 It was well known form the prior art that C-terminal truncations of human alpha interferon have not effect on the biological activity of the polypeptide (e.g. D1, page 54, 1st column, 1st paragraph; D2, page 21, lines 20-31; D3, page 6186, 1st column, last paragraph).

2.4 In view of the prior art and in the absence of any surprising technical effect the provision of further C-terminal truncated versions of human alpha interferon cannot be considered involving an inventive step. Claims 1 - 34 do therefore not meet the requirements of Article 33(3) PCT.